

DERWENT-ACC-NO: 2003-513643

DERWENT-WEEK: 200629

COPYRIGHT 2010 DERWENT INFORMATION LTD

TITLE: New human molecules for disease detection and treatment (MDDT), useful for diagnosing, treating and preventing diseases or conditions associated with the aberrant MDDT expression e.g. cancer, AIDS, atherosclerosis, epilepsy, or infections

INVENTOR: AZIMZAI Y; BAUGHN M R ; BECHA S D ; BHATIA U ; BLAKE J J ; BOROWSKY M L ; BURFORD N ; BURRILL J D ; CHANG H ; CHAWLA N K ; CHIEN D ; ELLIOTT V S ; EMERLING B M ; GANDHI A R ; GIETZEN K J ; GORVAD A E ; GORVARD A E ; HAFALIA A J A ; HO A ; HONCHELL C D ; ISON C H ; JIN P ; KABLE A E ; KHAN F A ; KHARE R ; LEE E A ; LEE S ; LEE S Y ; LEHR-MASON P M ; LU D A M ; MARQUIS J P ; NGUYEN D B ; RAMKUMAR J ; RICHARDSON T W ; RING H Z ; SPRAGUE W W ; SWARNAKAR A ; TANG Y T ; THANGAVELU K ; TRAN U K ; WARREN B A ; YUE H ; ZHENG W

PATENT-ASSIGNEE: INCYTE GENOMICS INC[INVT]

PRIORITY-DATA: 2002US-363649P (March 8, 2002) , 2002US-353284P (February 1, 2002) , 2002US-350410P (January 18, 2002) , 2001US-342052P (December 18, 2001) , 2001US-334182P (November 28, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE
<u>WO 03046152 A2</u>	June 5, 2003	EN
AU 2002359567 A1	June 10, 2003	EN
EP 1487989 A2	December 22, 2004	EN
AU 2002359567 A8	November 3, 2005	EN

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR

APPLICATION-DATA:

PUB-NO	APPL-DESCRIPTOR	APPL-NO	APPL-DATE
WO2003046152A2	N/A	2002WO-US38446	November 25, 2002
AU2002359567A1	N/A	2002AU-359567	November 25, 2002
AU2002359567A8	N/A	2002AU-359567	November 25, 2002
EP 1487989A2	N/A	2002EP-794113	November 25, 2002
EP 1487989A2	Based on	2002WO-US38446	November 25, 2002

INT-CL-CURRENT:

TYPE	IPC	DATE
------	-----	------

CIPS C07K14/47 20060101
CIPS C12N15/12 20060101

RELATED-ACC-NO: 2002-627559 2002-657522 2002-674945 2002-713444 2002-713453
2002-723340 2002-723448 2003-058385 2003-058429 2003-058518 2003-092996
2003-093118 2003-120469 2003-120667 2003-120774 2003-120797 2003-129423
2003-129519 2003-140448 2003-140453 2003-167112 2003-210247 2003-210353
2003-239519 2003-268197 2003-268319 2003-268321 2003-278569 2003-278643
2003-313243 2003-313247 2003-354596 2003-354597 2003-363137 2003-363142
2003-363161 2003-371995 2003-393436 2003-403125 2003-421156 2003-421159
2003-421277 2003-430274 2003-449567 2003-505207 2003-513744 2003-514037
2003-532894 2003-532903 2003-533003 2003-533016 2003-559157 2003-636761
2003-671468 2003-679949 2003-689669 2003-697610 2003-722079 2003-779081
2003-788347 2003-804054 2003-833535 2003-845310 2003-865587 2004-011523
2004-022653 2004-022655 2004-035124 2004-053042 2004-062335

ABSTRACTED-PUB-NO: WO 03046152 A2

BASIC-ABSTRACT:

NOVELTY - An isolated polypeptide (I), is new.

DESCRIPTION - An isolated polypeptide (I) comprises:

- (a) any of the 69 fully defined sequences of 36-1449 amino acids given in the specification;
- (b) a naturally occurring amino acid sequence at least 90% identical to 60 sequences from (a), at least 92% identical to 126, 756 or 359 amino acids, at least 96% identical to 1449 or 957 amino acids, at least 94% identical to 715 or 120 amino acids, at least 91% identical to 1442 amino acids, or at least 93% identical to 569 amino acids; or
- (c) a biologically active or immunogenic fragment of the polypeptide in (a).

INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated polynucleotide encoding (I);
- (2) a recombinant polynucleotide comprising a promoter sequence operably linked to the polynucleotide in (1);
- (3) a cell transformed with the recombinant polynucleotide;
- (4) transgenic organism comprising the recombinant polynucleotide;
- (5) producing or purifying (I);
- (6) an isolated antibody, which specifically binds to (I);
- (7) an isolated polynucleotide (II), comprising:
 - (a) any of the 69 sequences of 616-7783 bp, given in the specification;
 - (b) a naturally occurring polynucleotide sequence at least 90% identical to 65 sequences from (a), 97% identical to 1453 or 1625 bp, at least 91% identical to 703 bp, or at least 99% identical to 2220 bp;
 - (c) complements of (a) or (b); or

- (d) an RNA equivalent of (a)-(c);
- (8) an isolated polynucleotide comprising at least 60 contiguous nucleotides of (II);
- (9) detecting a target polynucleotide or (I) in a sample;
- (10) compositions comprising the polypeptide, an agonist compound, an antagonist compound or an antibody, and an excipient;
- (11) treating diseases or conditions associated with decreased expression or overexpression of functional MDDT;
- (12) screening for a compound that is effective as an agonist or antagonist of (I), that specifically binds to (I), that modulates the activity of (I), or is effective in altering expression of the target polynucleotide;
- (13) assessing toxicity of a test compound;
- (14) a diagnostic test for a condition or disease associated with the expression of MDDT in a biological sample;
- (15) diagnosing a condition or disease associated with the expression of MDDT in a subject;
- (16) preparing a polyclonal or monoclonal antibody with the specificity of the antibody in (6);
- (17) a polyclonal or monoclonal antibody produced by the method in (16);
- (18) compositions comprising the polyclonal or monoclonal antibody, and a carrier;
- (19) generating an expression profile of a sample containing the polynucleotides; and
- (20) an array comprising different nucleotide molecules affixed at distinct physical locations on a solid substrate, where at least one nucleotide molecule comprises a first oligonucleotide or polynucleotide sequence specifically hybridizable with at least 30 contiguous nucleotides of the target polynucleotide.

Gene therapy.

USE - The polypeptides and polynucleotides are useful in diagnosing, treating and preventing diseases or conditions associated with the decreased expression or overexpression of MDDT, such as cell proliferative (e.g. cancer, atherosclerosis), neurological (e.g. epilepsy, Huntington's disease, stroke), immune/inflammatory (e.g. AIDS, allergies) and developmental (e.g. Hypothyroidism, Cushing's syndrome) disorders, or infections. These are also useful in assessing the effects of exogenous compounds on the expression of nucleic acid and amino acid sequences of MDDT. The MDDT or its fragments are useful in screening compounds for effectiveness as agonist or antagonist of the polypeptides, or in altering the expression of the target polynucleotide and compounds that specifically bind to or modulate the activity of the polypeptide. The microarray is useful in monitoring or measuring protein-protein interactions, drug-target interactions, and gene expression profiles.

EQUIVALENT-ABSTRACTS:

BIOTECHNOLOGY

Preferred Method: Producing (I) comprises culturing the cell in (3) under conditions suitable for the expression of the polypeptide; and recovering the expressed polypeptide. Detecting a target polynucleotide in a sample comprises hybridizing the sample with a probe comprising at least 20 contiguous nucleotides comprising a sequence complementary to the polynucleotide in the sample, where the probe specifically hybridizes to the target polynucleotide to form a hybridization complex between the probe and the target polynucleotide or its fragments; or amplifying the target polynucleotide or its fragment using polymerase chain reaction amplification; and detecting the presence or absence of the hybridization complex, or the amplified target polynucleotide or its fragment, and optionally its amount, if present. Treating diseases or conditions associated with decreased expression of MDDT comprises administering to the patient the composition comprising the polypeptide or the agonist compound. In treating diseases or conditions associated with overexpression of MDDT, the composition comprising the antagonist compound is administered. Screening for a compound for effectiveness as agonist or antagonist of (I) comprises exposing a sample comprising the polypeptide to a compound; and detecting agonist or antagonist activity in the sample. Screening for a compound that specifically binds to (I) comprises combining the polypeptide with at least one test compound under suitable conditions; and detecting the binding of the polypeptide to the test compound to identify a compound that specifically binds to (I). Screening for a compound that modulates the activity of (I) comprises combining the polypeptide with at least one test compound under conditions permissive to the activity of the polypeptide; assessing the activity of the polypeptide in the presence of the test compound; and comparing the activity of the polypeptide in the presence of the test compound with the activity of the polypeptide without the test compound, where the change in activity of the polypeptide in the presence of the test compound indicates that the compound modulates the activity of (I). Screening a compound for effectiveness in altering the expression of a target polynucleotide comprises exposing a sample comprising the target polynucleotide to a compound under conditions suitable for the expression of the target polynucleotide; detecting altered expression of the target polynucleotide; and comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound. Assessing the toxicity of a test compound comprises treating a biological sample containing nucleic acids with the test compound; hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of (II) under conditions to form a specific hybridization complex between the probe and the target polynucleotide or its fragment in the biological sample; quantifying the amount of hybridization complex; and comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, where a difference in the amount of hybridization complex in the treated biological sample is indicative of the toxicity of the test compound. The diagnostic test for a condition or disease associated with the expression of MDDT in the biological sample comprises combining the biological sample with the antibody under conditions suitable for the antibody to bind the polypeptide to form antibody:polypeptide complex; and detecting the complex, where the presence of the complex correlates with the presence of the polypeptide in the biological sample. Preparing a polyclonal antibody comprises immunizing an animal with (I) or its immunogenic fragment under conditions to elicit an antibody response, isolating antibodies from the animal, and screening the isolated antibodies with the polypeptide to identify the polyclonal antibody, which specifically binds to the polypeptide mentioned above. Making a monoclonal antibody comprises immunizing an animal with (I) or its immunogenic

fragment under conditions to elicit an antibody response; isolating antibody producing cells from the animal; fusing the antibody producing cells with immortalized cells to form monoclonal antibody-producing hybridoma cells; culturing the hybridoma cells; and isolating from the culture the monoclonal antibody, which binds specifically to (I). Detecting the (I) comprises incubating the antibody with a sample under conditions to allow specific binding of the antibody and the polypeptide; and detecting specific binding that indicates the presence of the polypeptide in the sample. Purifying the polypeptide comprises incubating the antibody with the sample under conditions to allow specific binding of the antibody and the polypeptide; and separating the antibody from the sample and obtaining the purified polypeptide. Generating an expression profile of a sample, which contains the polynucleotide comprises labeling the polynucleotides of the sample; contacting the elements of the microarray with the labeled polynucleotides of the sample under conditions suitable for the formation of a hybridization complex; and quantifying the expression of the polynucleotides in the sample.

Preferred Antibody: The antibody is a chimeric, single chain, Fab fragment, (Fab')₂ fragment, or humanized antibody. The antibody is produced by screening a Fab expression library or a recombinant immunoglobulin library.

Preferred Composition: The composition comprising an antibody and an excipient, prefers that the antibody is labeled.

Preferred Array: The array is preferably a microarray. The array comprises a linker, which joins at least one of the nucleotide molecules to a solid substrate. Each distinct physical location on the substrate contains multiple nucleotide molecules having the same sequence at any single distinct physical location, and each distinct physical location on the substrate contains nucleotide molecules having a sequence, which differs from the sequence of nucleotide molecules at another distinct physical location on the substrate. The first oligonucleotide or polynucleotide sequence is completely complementary to at least 30 or 60 contiguous nucleotides of the target polynucleotide.

Dosage of the polypeptides, polynucleotides, antibodies, agonists or antagonists comprised in the composition is 0.1 microg-1 g. Administration can be oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, pulmonary, transdermal, subcutaneous, intraperitoneal, intranasal, enteral, topical, sublingual or rectal routes.

SPECIFIC SEQUENCES

Specifically claimed are human molecules for disease detection and treatment polypeptides comprising any of the 69 fully defined sequences of 36-1449 amino acids given in the specification. The polynucleotides encoding the polypeptides comprise any of the 69 sequences of 616-7783 bp fully defined in the specification.

Expression and purification were achieved using bacterial or virus-based expression systems. For expression, the cDNA was subcloned into an appropriate vector containing an antibiotic resistance gene and an inducible promoter that directs high levels of cDNA transcription. Recombinant vectors were transformed into suitable bacterial host, BL21 (DE3). Antibiotic resistant bacteria expressed MDDT upon induction with isopropyl beta-D-thiogalactopyranoside (IPTG). For purification, FLAG, an 8-amino acid peptide, enabled immunoaffinity purification using commercially available monoclonal and polyclonal anti-FLAG antibodies. Purified MDDT was obtained comprising any of the 69 sequences of 36-1449 amino acids, fully defined in the specification.

TITLE-TERMS: NEW HUMAN MOLECULAR DISEASE DETECT TREAT USEFUL DIAGNOSE PREVENT
CONDITION ASSOCIATE EXPRESS CANCER AID ATHEROSCLEROSIS EPILEPSY
INFECT

DERWENT-CLASS: B04 D16

CPI-CODES: B04-C01G; B04-E02F; B04-F0100E; B04-G01; B04-N04A0E; B11-C07A;
B11-C08E; B11-C08E3; B11-C08E5; B12-K04A; B12-K04E; B12-K04F;
B14-C03; B14-F02D1; B14-F07; B14-G01B; B14-G02A; B14-G03; B14-H01;
B14-J01A4; B14-J07; B14-N11; B14-N16; D05-H09; D05-H11; D05-H12A;
D05-H14; D05-H16; D05-H17A6; D05-H18B;

CHEMICAL-CODES:

Chemical Indexing M1 *01*

Fragmentation Code

M417 M423 M710 M720 M750 M781 N102 N135 N136 N161

P420 P431 P434 P442 P446 P520 P624 P625 P633 P814

P831 Q233 Q505

Specific Compounds

RA00H3

Registry Numbers

184616

Chemical Indexing M1 *02*

Fragmentation Code

M417 M423 M710 M720 M750 M781 N102 N135 N136 N161

P420 P431 P434 P442 P446 P520 P624 P625 P633 P814

P831 Q233 Q505

Specific Compounds

RA00H1

Registry Numbers

184611

Chemical Indexing M1 *03*

Fragmentation Code

M423 M710 M750 M781 N102 N134 N135 N161 P831 Q233

Q505

Specific Compounds

RA00NS

Registry Numbers

93605

Chemical Indexing M1 *04*

Fragmentation Code

M423 M710 M750 M781 N102 N134 N135 N161 P831 Q233

Q505

Specific Compounds

RA012P

Registry Numbers

105730

Chemical Indexing M1 *05*

Fragmentation Code

M417 M423 M710 N135 N136 N137 Q233

Specific Compounds

RA00GT

Registry Numbers

200757 200799

Chemical Indexing M1 *06*

Fragmentation Code

M417 M423 M710 M720 M781 N102 N137 N161 N163 Q233

Q508

Specific Compounds

RA00C8

Registry Numbers

184587

Chemical Indexing M6 *07*

Fragmentation Code

P431 P434 P442 P446 P520 P624 P625 P633 P814 P831

Q233 Q505 R515 R521 R535 R621 R624 R627 R633 R637

R639